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Systemic inflammation and cardiac surgery: insights from the RECCAS trial

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I read with great interest the RECCAS trial, in which the investigators explored the effects of intraoperative cytokine removal during cardiac surgery [1]. It addresses a critical issue: the modulation of systemic inflammation in cardiac surgical patients. The authors concluded that haemoadsorption (HA) did not result in significant reductions in cytokine levels on intensive care unit (ICU) admission or subsequently and observed no significant differences in organ dysfunction, ICU and hospital lengths of stay, or mortality rates. While the study provides valuable insights, certain aspects warrant further discussion to better contextualize the findings and implications.

The study population raises concerns regarding the generalizability and clinical relevance of the results. The inclusion of exclusively older patients (>65 years), with a mean age of 74 years, lacks a clear justification in the manuscript. Age is a key determinant of inflammatory response severity, with evidence suggesting that older adults exhibit reduced endothelial activation, impaired cytokine signaling, and attenuated innate immune responses, as highlighted in sepsis-related studies [2]. Moreover, nearly half of the patients did not undergo bypass surgery, valve surgery, or a combination of both, which differs significantly from the populations typically reported in cardiac surgery trials [3, 4]. Understanding the types of surgical procedures performed is essential, as surgical type may have a significant impact on systemic inflammation. Additional information regarding surgical type could provide deeper insights.

Blinding is another methodological aspect that requires clarification. Procedural interventions such as HA introduce inherent challenges to blinding to surgeons, particularly due to the visible presence of additional equipment in the operating theatre. The trial does not specify how performance bias was mitigated under these circumstances. Furthermore, details regarding the use of concurrent anti-inflammatory treatments, such as glucocorticoids, or the amount of blood transfusion administered during the perioperative period are absent. Both factors could profoundly influence systemic inflammation and may have confounded the study's outcomes.

With respect to outcomes and analysis, the selection of IL-6 levels on ICU admission as the primary outcome, while relevant to systemic inflammation, may have limited clinical relevance. Additionally, the lack of assessment of key organ-specific biomarkers, such as creatinine and bilirubin, limits insight into complications like acute kidney injury or liver dysfunction after surgery. Other inflammatory markers, such as C reactive protein, while being non-specific, could offer important insights into the degree of acute inflammation. Furthermore, the statistical analysis did not adhere to the intention-to-treat principle, with one participant excluded after randomization, which raises concerns about potential biases or systematic errors considering a small sample size.

The modulation of systemic inflammation during cardiac surgery remains a topic of considerable research interest. As the authors briefly discussed in

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their discussion, patient selection is likely a critical factor in determining the efficacy of HA. Risk factors such as advanced age, preoperative comorbidities, surgical type, and intraoperative perfusion parameters should be carefully considered. Evidence from anti-inflammatory treatments in cardiac surgery suggests that benefits may be most pronounced in patients at high risk of organ dysfunction driven by dysregulated inflammation [5]. A phenotype-based approach may therefore be crucial when evaluating the role of immunomodulatory therapies. Additionally, systemic inflammation in cardiac surgery is a complex process mediated by factors beyond cytokines, involving intricate interactions between immune cells and endothelial function [6, 7]. A comprehensive assessment of immune profiles, including complement activation and immune cell profile, in patients undergoing HA could further elucidate its mechanisms of action and potential benefits. Such assessments would provide more understanding of the immunologic effects of HA and may guide its use in future studies.

In conclusion, the RECCAS trial represents an important contribution to the growing body of literature on systemic inflammation management in cardiac surgery. Addressing the methodological considerations and providing a more detailed immunologic characterization of patients will be essential to advancing this field.

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Minghao Luo wrote the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Conflict of interest
The authors declare no competing interests.

Ethical approval and consent to participate
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